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## Dose-volume effects in rat spinal cord irradiated with protons

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## Chapter 3

# The setup and dosimetry

### 3.1 Introduction

For the irradiation experiment proton beams of 150 MeV were used. These were accelerated by the AGOR cyclotron. After extraction from the cyclotron, the beam was guided to the target area. The proton beam energy was not degraded or modulated.

In this chapter the beam line and setup used for the experiments will be described. Attention will be paid to the techniques used for dose administration and insight will be given in the accuracy of the dose administration. Other subjects dealt with will be the dosimetry of the small irradiation fields and the positioning of the rat in the beam. More details on the properties of the small irradiation fields used, will be given in chapter 4.

### 3.2 The beam line

A homogeneous irradiation field with an 80 mm diameter was obtained by a dual scattering system [70], consisting of a flat lead foil (1.44 mm thick) and a tungsten foil which decreases in thickness from the beam axis towards the edges (maximum thickness 1.03 mm). A plot of the thickness of this foil as a function of the radius is shown in figure 3.1. This shape is chosen to obtain a uniform dose distribution [70]. The distance between the scatter foils is 35 cm. A collimator between the scatter foils confines the beam radius to the radius of the second foil.

To obtain a uniform dose distribution, it is very important that the center of the beam is positioned on the center of the second scatter foil. A test was performed to check for the tolerance of this positioning. Using a horizontal bending magnet (“B4”) approximately 6.1 meters upstream the scatter system, the horizontal position of the beam at the position of the second scatter foil was varied. In figure 3.2 horizontal beam profiles found for different beam positions are shown. On the right side of the plot an increase in dose is seen in both

the well aligned profile and the +2.5 mm misaligned beam profile. This is due to an imperfection of the second scatter foil, but has no influence on the dose distribution in the center of the field. The main effect of displacement of the beam at the position of the second scatter foil is the increase and decrease of this artifact in addition to a tilt of the dose distribution. The result of an increase is an increase of the total proton flux through the ion chambers (see section 3.3), resulting in more monitor units at the same dose in the center of the field. This causes the dose in the center of the field to drop by 3.3% for +2.5 mm displacement. The same effect causes a rise of 0.4% when the beam is misaligned to -1.0 mm.

In figure 3.2 the dotted lines indicate the region that is used for the dose-volume effect experiments. A small misalignment of the beam has a minimal influence on the symmetry of the dose distribution in that region. The largest deviation is again found for a +2.5 mm misalignment. The difference between the dose on the left and right side was 3%. In the well aligned profile this is about 0.5% and in the -1.0 mm case the profile was found to be symmetric within the 1% measurement accuracy.

An overview of the layout of the beam line is given in figure 3.3. In the radiobiology experiments, the rat spinal cord is positioned 15 cm downstream of the final, field-shaping collimator. In this work this position is referred to as the isocenter. The final 45 mm thick brass collimator is referred to as “the patient collimator”. The distance from the rat to the virtual proton source, located approximately half way between the two scatter foils, is 2.9 m. Between the second scatter foil and the patient collimator several additional collimators are placed to intercept tails of the beam and to confine the beam to the outer

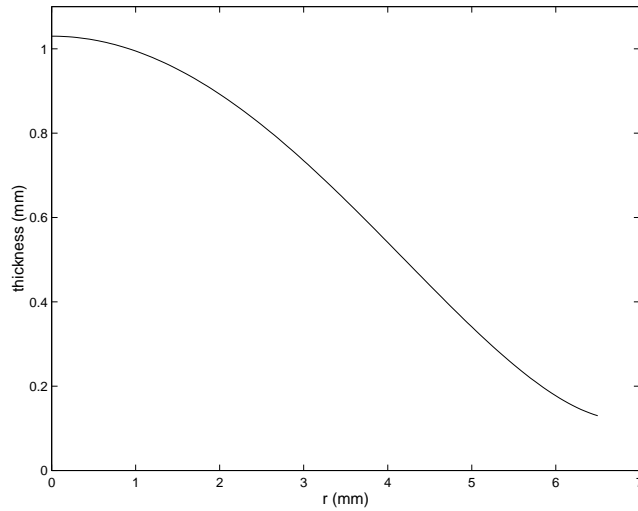


Figure 3.1: Thickness of the second scatter foil vs. the radius

maximum radius of the patient collimator. In chapter 4 it will be shown that air scatter and not the direction of the collimator edges, determines the size of the penumbra. Therefore the edges of the patient collimator were made parallel.

The aim of the experiments described in this thesis was to investigate the dependence of the tolerance dose on the size of the irradiated region (field size)

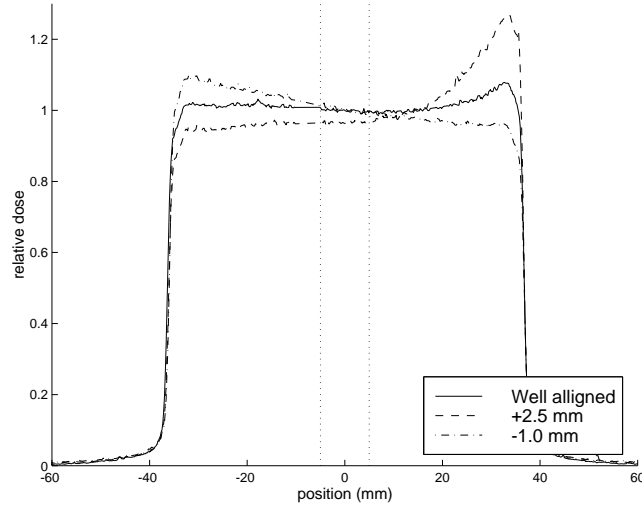


Figure 3.2: Beam profiles measured for three different situations. The solid line shows the relative dose distribution if the beam was well aligned to the second scatter foil. The dashed line shows the relative dose distribution that occurs when the beam is misaligned to +2.5 mm. The dash-dotted line shows the result of a -1.0 mm misalignment. The vertical dotted lines indicate the 10 mm region, which is used in the dose-volume experiments.

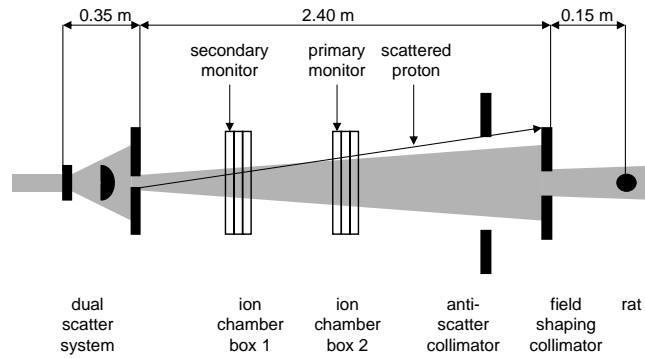


Figure 3.3: Schematic overview of the dedicated radiobiology beam line

and the shape of the dose distribution. Therefore, many different beam shapes have been used. Beam shaping is done by appropriate patient collimator shapes. Field sizes ranged from  $2 \times 10 \text{ mm}^2$  to  $20 \times 20 \text{ mm}^2$ .

### 3.3 Dose administration

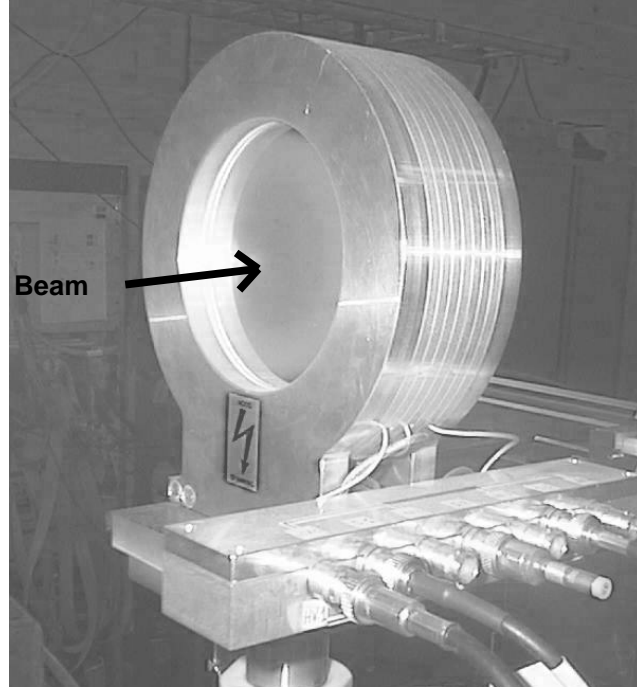


Figure 3.4: The primary ion chamber, used for monitor-unit measurement during the irradiation.

In the beam line two independent dose monitors (“primary” and “secondary”) were used to register the administered dose in monitor units (see figure 3.4). Both monitors are in separate ion-chamber boxes, each consisting of 6 parallel plate chambers (gap = 5 mm). Within the boxes the 6 chambers are separated by aluminated mylar foils. On 4 foils a high voltage of at least 1.2 kV was applied. The signal on the anode is collected from the gaps on both sides of the anode foil.

The collection efficiency of the electron-ion pairs depends on the high-voltage. To test whether the high-voltage applied to the foils results in 100% efficiency, both monitors were tested with different high voltage values. This experiment was carried out for two different dose rates: 20 Gy/minute, which is the dose

rate used in the biological experiments and 70 Gy/minute to check the monitors for robust operation.

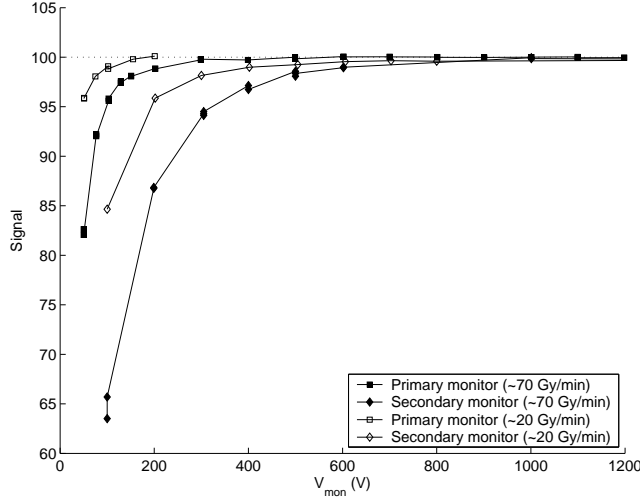


Figure 3.5: Dose monitor response as a function of applied high voltage.

The measured collection efficiencies are shown in figure 3.5. In this experiment every data sample was taken with one monitor at 2 kV and the other varying. The response of each monitor was first normalized to the other monitor running at 2 kV and then to its own normalized response at 2 kV and at a dose rate of 70 Gy/minute. From figure 3.5 it can be seen that even at a dose rate of 70 Gy/minute, the collection efficiency is 100% at 0.8 kV. This shows that the minimum operating voltage of 1.2 kV is sufficiently high.

The current produced by ionizations of air in the ion chamber is fed to a current-to-voltage converter (QSX, TRIUMF, Canada). A voltage to frequency converter (Hytec, NVFS 2504) converts the resulting voltage into a pulsed signal (NIM pulses). The frequency of these pulses is proportional to the voltage. A level translator (Phillips, level translator model 726) converts the NIM pulses to TTL pulses. These are registered by a counter on a PC card (National Instruments, Woerden (NFL), PC-TIO-10). The maximum voltage that the current-to-voltage converter can produce is 10 V. This corresponds to a pulsed output signal of 1 Mhz which is fed to the counter in the PC. The readout electronics, the function of different monitor segments and the amplification factors of the different channels are summarized in figure 3.6.

In the injection line between the ion source and AGOR an electrostatic beam-stop (ESB) was installed. Before the beam enters AGOR, it needs to be bent from a horizontal to a vertical direction. This is done using a strong electric field between a set of plates (see figure 3.7). The voltage on the plates that creates this field is  $\sim 3700$  V. Reducing this voltage by 500 V already results

in sufficient deflection to prevent the beam from entering AGOR (closed ESB). During the experiments the natural state of the high voltage is 1 kV less than the voltage required to get beam on target. To start the irradiation the high voltage is set at its “open” value to allow passage of the beam (open ESB).

The beam line is controlled by a PC running Labview<sup>tm</sup>. The irradiation is started by opening the ESB. During the irradiation the integrated beam current as well as the ratio of the differential readout of the two beam monitors are monitored. When the preset number of monitor units is reached, the beam is switched off by closing ESB. Overshoot measurements showed that the maximum overshoot in time was 15 ms (see figure 3.8). Usually a dose rate of 15-20 Gy/min was used which means the dose overshoot due to the reaction time

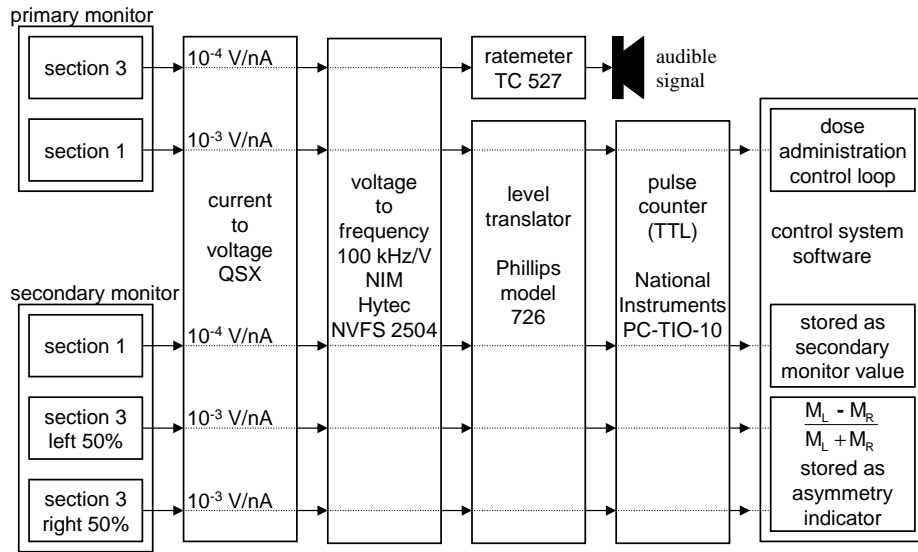


Figure 3.6: Dose-monitor signal handling.

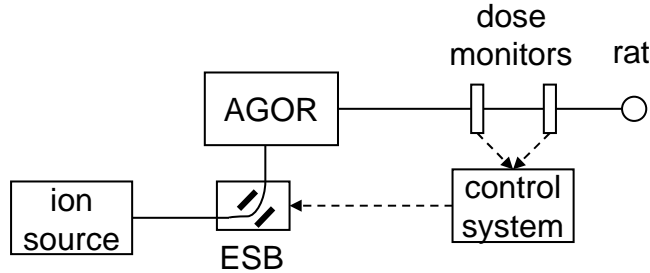


Figure 3.7: Schematic overview of the control of the dose administration

of the control system and the beam stop is at most 0.06 Gy. This maximum overshoot dose is negligible compared to the doses used. The ratio of the differential signals of both monitors is used to verify that both monitors produce a consistent readout. The number of monitor units registered by the primary and secondary dose monitors was recorded in a log file for later analysis.

### 3.4 Absolute dosimetry

A dose monitor only gives a number proportional to the number of protons that passed through it. This monitor reading needs to be calibrated to dose at the location of the spinal cord of the rat that is irradiated.

A PTW30001 Farmer chamber is used as a primary standard [71] for monitor-unit calibration. A beam of  $\varnothing 70$  mm has been used, because the farmer chamber must be irradiated uniformly. This farmer chamber was placed in a polystyrene phantom to simulate the material upstream of the rat spinal cord.

A scintillating screen [72, 73] was used to measure relative dose distributions of both the large ( $\varnothing 70$  mm) and the small fields with the same number of monitor units. Upstream of the screen, 3 cm polystyrene was placed to simulate the amount of material upstream of the rat spinal cord during the irradiations. The ratio of the light output in the center of a small field and the center of the large field was used to correct the amount of MU's to be applied in the small field, so that the desired dose is given in fields much smaller than the farmer chamber. The characteristics of the scintillating screen setup and the spatial energy/flux properties of the beam will be described in more detail in section 4.

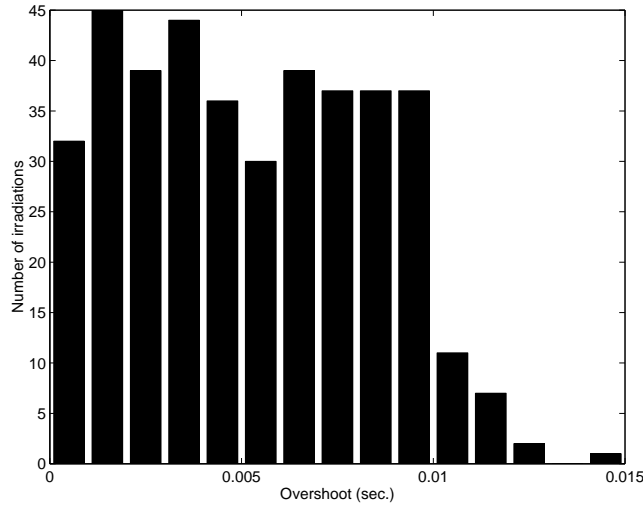


Figure 3.8: Overshoot times measured during experiment PTP-3



### 3.5 Positioning

We used a Lucite frame to position the rats in the radiation field. In this frame, 6 anesthetized rats were positioned vertically with the base of the skull and the neck fixed and with 5 cm distance between the spinal cords of different animals. Fixation is achieved by placing the animal with the base of the skull on a 5 mm thick Lucite support with a semi-circular hole. After closing the hole the neck is fixed immediately above the target volume. This setup is depicted in figure 3.9.



Figure 3.9: Six rats positioned in the Lucite frame on the remote controlled slider.

The irradiations were performed in the cervical spinal cord (C1-T2) and the center of the field was in most experiments positioned at C4.

In most experiments the dose distribution was homogeneous in the lateral direction and therefore chosen to be quite large (10 mm) in that direction. In these experiments the lateral positioning was not very critical as the spinal cord width (approximately 3.5 mm) was much smaller than the lateral field size (10 mm).

A typical experiment to establish a dose-effect curve with reasonable statistical accuracy, requires irradiation of 30-40 rats. Therefore, much effort has been put into automating the procedure and enabling remote control of the equipment. To achieve this, the Lucite frame was placed on a slider that could be moved using a remotely controlled stepping motor.

For experiments in which the dose distribution was inhomogeneous in the lateral direction, a more sophisticated positioning technique using X-ray radiography was used. This will be described in more detail in chapter 7.